REMARKS

The present invention relates to methods of distinguishing P-gp or MRP mediated multiple drug resistance from BCRP multiple drug resistance.

Reconsideration and allowance of the application are respectfully requested in light of the foregoing amended claims and the following remarks.

Claims 13-28 and 57-59 are pending in this application. Claims 16, 21-22, 27 and 57-59 have been canceled. Claims 13, 15, 18-20 and 24 have been amended.

The Examiner has rejected claims 57-59 under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expressions "$R_7NH(CH_2)_v$ or ..." and R_7 is H or ..." and R_8 is selected is from..." .....are not understood since there are no R_7 and R_8 in the formula I..... . Cancellation of claims 57-59 renders the rejection under 35 USC 112 second paragraph moot.

The Examiner has rejected claims 13, 15, 17-18, 20, 23-24, 26 and 28 under 35 USC 102(b) as being anticipated by Abe et al. (Br. J. Cancer, 1995, 72, page 418-423, PTO-1449) and has further rejected claims 13-15, 17-20, 23-26 and 28 under 35 USC 102(b) as being anticipated by Tasaki et al. (J. Urology, 1995, 154, page 1210-1216).

Applicants respectfully traverse the 35 USC 102(b) rejections in view of amended claims 13, 15, 18, 20 and 24. Applicants have amended claims 13, and 24 to overcome the Abe et. al. and Tasaki et al. references by particularly pointing out the chemosensitizing reversal agents as those of Formula (I), Fumitremorgin A, Fumitremorgin B and Fumitremorgin C. In addition applicants have amended claim 13, 18 and 24 to define the specific cell lines used as S1-B1-20, HL-60/AR and S1-M1-3.2. Applicants have further defined the chemotherapeutic agents in dependent claim 15 as selected from mitoxantrone, doxorubicin, paclitaxel and topotecan and in dependent claim 20 as selected from mitoxantrone and doxorubicin.

Applicants believe they have overcome the 35 USC 102(b) rejections of Abe et al and Tasaki et al by defining the undisclosed or anticipated specific cell lines S1-B1-20, HL-60/AR and further defining resistant cancer cell line S1-M1-3.2. Additionally, also defined are the chemosensitizing reversal agents as those of Formula (I), Fumitremorgin A, Fumitremorgin B and Fumitremorgin C and the chemotherapeutic agents as those defined in amended dependent claims 15 and 20 and as further defined in claim 26.

Abe describes two MRP expressing cell lines called T98G and IN500. Abe further uses an MDR-1(Pgp) expressing cell line called CCF-STTG-1 and an additional cell line IN-157 which does not express Pgp or MRP. The IN-157 is not a multiple drug resistant cell line, but is a control for the drug resistant cells. Abe looks for chemosensitizing agents for Pgp and MRP multiple drug resistant cells which is different from the instant invention which is BCRP resistance.

The Abe et al reference evaluates the ability of various compounds to resensitize drug resistant cells that overexpress MDR-1 or MRP. The instant invention focuses on cell lines

which develop resistance by the BCRP pathways. The Abe reference has a different type of resistance which is PgP or MRP multiple drug resistance. In contrast, the instant invention focuses on BCRP resistance.

The cell line of the Tasaki et al reference expresses MRP which is not the phenotype in the instant invention, BCRP.

The cell line of the instant invention expresses neither PgP or MRP multiple drug resistance but expresses BCRP and is therefore distinct from the art.

It is the applicants view that the the Tasaki et al reference does not inherently distinguish PgP or MRP multiple drug resistance from BCRP because the Tasaki et al reference only distinguishes between PgP and MRP multiple drug resistance: while the present invention however, distinguishes between PgP or MRP multiple drug resistance and BCRP multiple drug resistance.

In addition, it is the applicants view that the Abe et al reference does not inherently distinguish PgP or MRP multiple drug resistance from BCRP because the Abe et al reference evaluates the ability of various compounds to resensitize drug resistant cells that overexpress MDR-1 or MRP. The present invention however, focuses on cell lines which develop resistance by specifically BCRP pathway.

Applicants respectfully request the Examiner to reconsider, withdraw the 35 USC 102(b) rejections and allow the claims.

The Examiner has rejected claims 16, 21, 27 and 57-59 under 35 USC 103(a) as being anticipated by Tasaki et al. (J. Urology, 1995, 154, page 1210-1216) and Cui et al. (PTO-892). Cancellation of claims 16, 21, 27 and 57-59 renders the rejection under 35 USC 103(a) moot.

Applicants have further submitted an amendment petition under 37 CFR 1.48(b) to remove the name of Maya Prakash Singh as an inventor as he is not a co-inventor of the subject matter embraced by this application.

In conclusion, applicants respectfully request that the Examiner enter the amendment, reconsider the rejections in light of the remarks herein, amendments to the claims, and allow the application. Favorable treatment is earnestly solicited.

Respectfully submitted,

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